REMARKS

Amendments to the Claims

Claims 1 and 4 have been amended without prejudice and new claims 13 and 14 have been introduced to recite preferred embodiments of applicants' invention that are more clearly differentiated from the prior art.

Amended claim 1 incorporates the limitation recited in original claim 2 and at page 10, line 22-23 which specifies that the first and second supply sources supply at least 1000 microfluidic reactors arranged in parallel via an upstream channel or channels.

Amended claim 1 further incorporates the limitation recited in original claim 6 that for all the reactors, the resistance of each of its upstream channels is at least 10 times larger than the resistance of the downstream channel or channels.

Amended claim 4 specifies that the resistance of all the upstream channels is at least 100 times larger than the resistance of the downstream channels (page 9, lines 22-24).

New claim 13 specifies that the microfluidic system according to claim 1, comprises at least the following 3 layers (page 12, line 8):

(i) an inlet/outlet layer comprising inlet channels for first and second fluid supply source and at least one outlet channel (page 12, lines 9-20);

(ii) a connecting layer comprising a plurality of side channels with varying diameter and/or length (page 12, line 22-32); and

(iii) a microfluidic layer, which comprises microfluidic reactors which are connected to the connecting channels via a port and through the connecting channels are in fluid connection with the inlet and outlet channels of the inlet/outlet layer (page 13, lines 1-10).

New claim 14 specifies that the system recited in new claim 13 comprises a plurality of connecting layers connecting a plurality of microfluidic layers to a single inlet/outlet layer (page 14, lines 5-7).

Claim Rejections – 35 USC § 112

Claim 2 was rejected under 35 USC § 112, first paragraph. The Examiner asserted that while the specification provided enablement for "first and second microfluidics reactors, it does not provide enablement for 1,000 microfluidis reactors". Applicants respectfully traverse this rejection.

Applicants disclose that their invention is specifically directed to *a fluid distribution system, allowing to feed several fluid phases to any number of parallel microfluidic units from a single or multiple source for each phase* (page 7, line 4-11).

Applicants disclose on page 10, lines 19-23 that *when used for numbering-up the number of microreactors will generally be from 1000 to 100000 and the number of feeding channels is adapted thereto. For example it could be at least 1000 or even at*

least 50000. Thus, one expressly taught aspect of the invention is a network including a large number of micro-reactors

The Examiner asserted that the specification is not enabling because it is not clearly stated how 1,000 reactors and channels are being connected. Applicants respectfully disagree.

Applicants teach several alternative approaches to constructing an apparatus have a plurality of micro-reactors.

Applicants teach, for example, on page 12 , line 8 to page 14, line 7 a microfluidic system that comprises at least 3 layers: an inlet/outlet layer comprising inlet channels for first and second fluid supply source and at least one outlet channel; a connecting layer comprising a plurality of side channels with varying diameter and/or length; and a microfluidic layer, which comprises the microfluidic reactors which are connected to the connecting channels via a port and through the connecting channels are in fluid connection with the inlet and outlet channels of the inlet/outlet layer.

The materials and method of fabrication used to construct the layers are disclosed. Applicants for example point out that in a preferred embodiment of the invention the microfluidic layers need only be etched on their surface, which may be made using a variety of *easily accessible microfabrication techniques*, including, but not limited to, wet and dry etching, molding, laser ablation.

Applicants teach two alternative embodiments of a microfluids network that can be scaled up to any number of reactors on page 14, line 9 to page 16, line 7 in combination with Figures 1 and 2.

Applicants, generalize the essential elements required for any number of reactors on page 15, line 14 to page 16, line 8.

The simple microfluidic network presented in Figure 1/2 can be generalized in the following way. A more complex microfluidic network involving the parallel action of at least 2 reactors receiving at least 2 different fluids from at least 2 external sources, with exactly one source per fluid, will require the following elements:

- *(i)* *inlets and outlets for the fluids*
- *(ii)* *"splitting node" splitting the fluids coming from the inlets to the various micro-processing elements.*
- *(iii)* *upstream channels, located between the split and the points where the various fluids meet. These upstream channels are optionally used in the processing, for example for cooling, heating, or otherwise processing the inlet fluids before they join.*
- *(iv)* *joining nodes, where the fluids from the at least two sources meet and start to interact; these joining nodes may be the reactors.*
- (v) *Downstream channels, located after the joining node, respectively after the reactors, and leading to either the outlets or any collecting channel or gutter which collects the output from the various processing elements. The downstream channels are optionally used to further process the at least two fluids together.*

Applicants' respectfully submit that the teachings summarized above and other teaching found in the specification would have provided adequate guidance to a person of ordinary skill in the relevant art to which the invention pertains (e.g., graduate physical chemist, chemical engineer or physicist with several years of experience in

fluids mixing) to design and construct a microfluids system having 1,000 micro-reactors or more.

For example the skilled person could design the network simply by starting with the apparatus diagrammed in Figure 1 and progressively add splitting nodes to the α and β paths (α1, α2, α3,.....and β1, β2, β3....) ending at joining nodes which could simply be the inlet of each mico-reactor (1, 2, 3, ...) The skilled person would then add downstream channel or channels for outflow from each micro-reactor (γ1, γ2, γ3,....pathways) which leads to either the outlets or any collecting channel or gutter which collects the output from the various processing elements.

The skilled person could choose to either fabricate the device from individual tubes, splitting nodes (e.g. "T" connectors) and micro-reactors (e.g. opposing nozzles). However, the specification teaches that a three-layer construction is preferable. Here a large number of channels or micro-reactors could be etched on an individual surface much like an integrated circuit board. Such fabrication methods are known.

In light of the above arguments, applicants respectfully request that the Examiner reconsiders and withdraws the §112, first paragraph rejection.

Claim Rejections – 35 USC § 103

Claim 1, 2, and 4-6 were rejected under 35 USC 103(a) as being unpatentable over Allen et al (WO 01/128670). Applicants' respectfully traverse this rejection.

Regarding claims 1 and 4, applicants submit that Allen et al does not present a case of *prima facie* obviousness under § 103(a) at least because Allen neither teaches nor suggests the first and second supply sources supplying *at least 1000 microfluidic reactors arranged in parallel* via an upstream channel or channels, said upstream channel or channels positioned before the microfluidics reactors, the reactors each having at least one downstream channel which is positioned after the reactors, wherein for *all the reactors, the resistance of each of its upstream channels is at least 10 (or 100) times larger than the resistance of the downstream channel or channels.*

Allen is directed to "a fluidic mixer that mixes two fluids without using mechanical stirrers. The two fluids are fed into an interaction cavity under predeterminable conditions that ensure the fluid flows <u>oscillate and feed in an alternating manner two exit channels</u>. The fluids in the exit channels form interleaved layers having widths related to the frequency of oscillation." (Abstract – emphasis added)

Thus, Allen is concerned with an individual reactor which is designed to osscilate its output stream between two exit channels. Allen is silent concerning the problem addressed by applicants, namely a microfluidics distribution system that feeds a large number of reactors, e.g., greater than 1000, that is stable to small pressure fluctuations in the distribution channels and shows reduced occurrence of multiphase shunts.

Applicants found that "when the resistance of the upstream channel or channels is 10 times higher, preferably 100 times higher than the resistance of the down stream channel or channels, the influence of small variations in flow rate in either of these channels is limited and hence a more robust system is provided". Page 9, lines 15-20 and 22-4.

Allen is silent about the influence of the relative resistance of liquids in upstream and downstream channels when connecting many parallel reactors, let alone that the resistance of *each of its upstream channels being at least 10 (or 100) times larger than the resistance of the downstream channel or channels.*

Because it is well known in the art of fluid dynamics that varying cross-sectional dimensions results in varying flow rates, the Examiner asserted that it would have been obvious to one having ordinary skill in the art at the time of the invention to have modified the channel dimensions to increase the resistance of upstream channels at least 10 or 100 times (claim 4) larger than the resistance of the downstream channels to change the flow rate to modify mixing and reaction rate of fluids.

However, if the motivation to modify channel dimensions were solely based on the desire *to modify mixing and reaction rate of fluids,* applicants submit that the artisan could equally well have reduced the dimensions of some of the downstream channel to achieve an equal or higher resistance than some or all of the upstream channels. This arrangement is in fact taught by Allen in **Fig 6** where downstream from mixer **612** is channel **616** and channels **624**, e.g., the resistance of channel **624** is higher than the corresponding upstream channel.

Allen does not deal with a system that involves distributuion to a large number of micro-reactors, is silent regarding the problem of instability in such a system, and offers no guidance how this problem is solved. Applicants respectfully submit that the Examiner has used the knowledge gained from applicants' disclosure as a blueprint to reconstruct their claimed invention from the disclosure of Allen. This approach contravenes the statutory mandate of §103 which requires judging obviousness at the point in time when the invention was made. *Grain Processing v. American Maize-Prods. Co.*, 840 F.2d 902, 907 (Fed. Cir. 1988).

Claim 13 and 14 are even further removed from Allen because they disclose additional features not taught or suggested by Allen.

Claim 13 recites a microfluidic system according to claim 1 comprising at least 3 layers: inlet/outlet layer; connecting layer; microfluidic layer, while claim 14 specifies a plurality of connecting layers connecting a plurality of microfluidic layers interfacing with a single inlet/outlet layer. Although, Allen mentions that a plurality of the fluidic mixers can be utilized such as the two-stage arrangement shown in Fig 6, Allen does not disclose arranging the system in three layers, nor in a plurality of layers.

In view of the foregoing amendment and remarks, applicants respectfully request that the application be allowed to issue.

If a telephone conversation would be of assistance in advancing prosecution of the subject application, applicants' undersigned agent invites the Examiner to telephone him at the number provided.

Respectfully submitted,

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